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Epidemic Human Immunodeficiency Virus (HIV) Infection Among Intravenous Drug Users (IVDU)

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Human immunodeficiency virus (HIV) infection is epidemic among intravenous drug users (IVDU), particularly in the northeastern United States. IVDU are playing a critical role in the spread of HIV by infecting their heterosexual partners and children, as well as their needle-sharing partners. The epidemiology of HIV infection among IVDU is reviewed here, including a compilation of seroprevalence data. Relevant determinants of the future spread of HIV among IVDU are discussed, including the major risk factors for HIV seropositivity, the modes of HIV transmission, and aspects of the natural history of HIV infection in IVDU. The public health policy implications of these issues include the need for education of adolescents and the general public about the risks of drug injection and heterosexual intercourse with IVDU, as well as motivation of IVDU to stop injecting, never share injection paraphernalia, or, at least, clean needles effectively.

INTRODUCTION

Infection with the human immunodeficiency virus, type 1 (HIV-1; also called HTLV-III, LAV-1, and ARV; referred to here as HIV), the etiologic agent of the acquired immunodeficiency syndrome (AIDS), is epidemic among certain segments of the United States population, including intravenous drug users (IVDU). The proportions of the total of 31,381 reported AIDS cases in the U.S. attributed to the two major transmission categories, male homosexual activity and intravenous (IV) drug use, have remained constant over the past few years at 66 percent and 17 percent, respectively [1]. In Connecticut, however, newly diagnosed AIDS cases are now predominantly relaed to IV drug use [2].

In Connecticut, as well as in New York and New Jersey, the percentage of AIDS cases involving IV drug use has been steadily increasing over the past few years. Thirty-eight percent of the AIDS cases reported in Connecticut in 1986 were in IVDU and an additional 4 percent were in IVDU who were also homosexual/bisexual males; only 40 percent of the Connecticut AIDS cases reported in 1986 were among those whose only risk for acquiring HIV was a homosexual/bisexual sexual orientation [2]. New Haven, Connecticut, has the highest cumulative incidence rate of AIDS cases

Abbreviations: AIDS: acquired immunodeficiency syndrome ARC: AIDS-related complex ARV: AIDS-related retrovirus CDC: Centers for Disease Control CMV: human cytomegalovirus EBV: Epstein-Barr virus EIA: enzyme-linked immunoassay *gag:* group-specific antigen HIV-1, HIV: human immunodeficiency virus, type 1 HTLV-I, HTLV-II, HTLV-III: human T-lymphotropic virus, types 1, 2, and 3, respectively IV: intravenous IVDU: intravenous drug users LAV-1, LAV: lymphadenopathy-associated virus USPHS: United States Public Health Service WB: Western blot

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among Connecticut cities and towns. About 60 percent of the 90 reported AIDS cases in the city of New Haven have been associated with heterosexual intravenous drug abuse [3]. These persons have been either IVDU, heterosexual partners of IVDU, or infant children of IVDU [3]. The cumulative incidence of AIDS in the city of New Haven (68/100,000) is still modest compared to the highest incidence areas of the city of San Franciso (316/100,000), western Palm Beach County, Florida (295/100,000), and the borough of Manhattan (270/100,000) [4]. The currently increasing HIV seroprevalence in New Haven, and the experiences in areas where the HIV epidemic is more advanced among IVDU (such as New York City and several European cities, discussed later), however, lead to gloomy predictions of a steadily increasing AIDS incidence in New Haven in the future. Indeed, the entire urban Northeast may be a harbinger for the evolution of this epidemic beyond, as well as among, U.S. IVDU to those who are not now considered at increased risk for acquiring HIV.

A major public health concern is HIV transmission from IVDU to their heterosexual partners and children. Four percent (1,180) of all U.S. AIDS cases (2 percent of males with AIDS and 27 percent of females with AIDS) have heterosexual sex partners with AIDS or at risk for AIDS as their only reported risk factor [1]. About 80 percent of all such cases of presumably heterosexually transmitted AIDS in the U.S. were apparently acquired by heterosexual contact with IVDU, predominantly from male-to-female transmission. In Connecticut, 65 percent (13/20) of such presumably heterosexually acquired AIDS cases were apparently transmitted from IVDU [2]. Accurate seroprevalence surveys in the general U.S. population have not yet been done, so it is currently impossible to assess how rapidly HIV infection might spread in the U.S. through heterosexual activity.

Only two large-scale HIV seroprevalence studies of groups not considered to include persons in currently recognized HIV transmission categories have been reported in the U.S. Nationwide, only 0.04 percent of voluntary blood donors were WB (Western blot)-confirmed seropositives [5]. Among military recruit applicants [6], however, there was greater geographic and racial variation in HIV seroprevalence, with rates of about 1 percent among the oldest, non-white recruit applicants from Mid-Atlantic states (including New York and New Jersey). It remains unclear how many of the military recruit applicants studied were IVDU and/or homosexual/bisexual males [6].

The epidemiology of pediatric AIDS is also closely linked to IVDU. Eighty percent (362/453) of the U.S. pediatric AIDS cases were acquired perinatally in families where one or both parents had a risk factor for AIDS [1], largely parenteral drug use. Most of these cases of apparently maternally transmitted pediatric AIDS are from New York City, where 84 percent of the known children with AIDS have one or both parents who are IVDU [7]. In New Haven, 87 percent of the 23 symptomatic cases of HIV infection in children have occurred in families where the mother or her sexual partner were IVDU [8]. Estimates are made that at least 500 HIV-infected infants are now born annually in New York City alone [7].

Despite the deadly reality and alarming potential of epidemic HIV infection among IVDU, thorough epidemiologic study has been limited by the isolated and stigmatized nature of the IVDU subculture. After reviewing the epidemiology and natural history of HIV infection among IVDU worldwide, including preliminary data from our ongoing studies in Connecticut and data presented at the International Conferences on AIDS in 1985 and 1986, the public health policy implications of this information will

be discussed. Emphasis will be placed on the factors that are most relevant in determining the degree to which HIV will spread in the future—prevalence of infection, sexual and drug use behaviors responsible for HIV transmission, and the role of cofactors in susceptibility to and outcome of HIV infection.

SERO-EPIDEMIOLOGY

The prevalence of HIV infection among those who use intravenous drugs has been estimated in the U.S. at between 5–75 percent with an annual incidence of 1–10 percent [9]. Estimates of the size of the total population at risk for HIV infection from intravenous drug use remain incomplete because of difficulties in defining and studying this population. There are also uncertainties about the nature and extent of the practice of different individuals re-using injection equipment ("needle sharing") which presumably underlies HIV transmission among IVDU. IVDU as a group are diverse and often anonymous. Generally, IVDU are only identified when arrested or when seeking drug abuse, psychiatric, or medical treatment. While the National Institute on Drug Abuse estimates 350,000–400,000 active intravenous heroin users (who self-inject largely at least daily), no precise estimates of the number of periodic casual users of heroin ("chippers") or of intravenous cocaine and amphetamine users are available [10]. Estimates are made, though, of 750,000 IVDU nationwide; data suggests that there are 258,000 IVDU in New York State [11]. All the published data on HIV infection in IVDU are currently limited to narcotic addicts.

The seroprevalence of HIV among IVDU has been studied in various groups of IVDU as they presented to the criminal justice and/or drug treatment systems, although all these data are biased by representing only discrete geographically and behaviorally defined subsets of IVDU that may not have uniform risk of HIV infection. Tables 1 through 3 list HIV seroprevalence rates—by enzyme-linked immunoassay (EIA) with a confirmatory test such as a Western blot in most cases, as indicated—from different groups of IVDU worldwide [12–64].

It is reasonable to posit that HIV risk among IVDU varies with the interrelated degree of drug abuse and needle sharing, and examination of Tables 1 through 3 supports such a speculation. The "detoxification" groups (in Table 1) include hospitalized IVDU who are "strung out" after heavy, intensive heroin abuse. These groups may be more similar to groups of IVDU hospitalized for other reasons (such as infections or other illnesses that are often related to unsterile injections and needle sharing) than to those on chronic methadone maintenance programs. Those on chronic methadone maintenance programs may still be injecting (often cocaine, rather than heroin), but are likely to be injecting drugs less intensively (i.e., perhaps sharing needles less) and more likely to have access to health care and AIDS risk reduction counseling. The studies identified as "hepatitis studies" in Tables 1 through 3 may select a subset that has active illness from another injection-acquired virus and may therefore be more likely than average to have acquired HIV by needle sharing. Those being admitted to methadone maintenance programs may more accurately reflect the full gamut of the population of active IVDU in a community. Persons seeking drug abuse treatment may, however, have a lower risk for HIV infection than those who do not voluntarily seek to limit their self-destructive behaviors, such as prisoners. Generally, to avoid selection bias in epidemiologic investigations and an overestimate of HIV seroprevalence, it seems prudent to study non-hospitalized IVDU in community-based settings.

TABLE 1
HIV Seroprevalence Among IVDU

Location/Group	% EIA + (No.)	% Confirmed + (No.)	[Ref] Date
New York City			
Detox.*	87 (75/86)	58 (50/86) (RIPA—p25)	[12] 1984
Detox. (while on Meth. Maint.)	72 (51/71)	—§	[13] 1985
Detox. (first time)	51 (32/63)	—§	[13] 1985
Meth. Maint.**	57 (80/140)	—§	[13] 1985
Hosp.***	—	56 (14/25) (WB)	[14] 1981–82
Meth. Maint.	—	29 (9/31) (WB)	[14] 1981–82
Detox. & Meth. Maint.	59 (162/273)	—§	[15] 1985
Detox. & Meth. Maint.	47 (166/351)	—§	[16] 1986
Hosp.	75 (6/8)	—	[17] 1985
Outpatient****	25 (5/20)	—	[17] 1985
Meth. Maint.	—	32 (141/443) (WB)	[18] 1985
Meth. Maint.	—	35 (36/103) (WB)	[19] 1984–85
Boston			
Meth. Maint. Admit.*****	9 (6/69)	42 (29/69) (WB)	[20] 1982–83
New Jersey			
Meth. Maint., Outpatient Drug-Free, and Residential Treatment	—	2–59 (total 745) (WB)	[21–23] 1984
New Haven			
Hepatitis study	30 (84/283)	10 (28/283) (WB)	[24] 1982–83
Meth. Maint. Admit.	23 (39/171)	22 (38/171) (WB)	[25] 1986
Miami			
Meth. Maint.	12 (23/186)	5 (9/186) (WB)	[26] 1986
San Francisco			
Detox. & Meth. Maint.	—	10 (28/284) (WB)	[27] 1985
—	9 (5/53)	—§	[13] 1985
Meth. Maint. & other	—	5 (6/128) (WB & IF)	[28] 1985
Chicago			
—	11 (4/35)	—§	[13] 1985
Washington, D.C.			
—	7 (—)	—§	[23] 1986
New Orleans			
—	<1 (—)	—§	[23] 1986
California (except San Francisco)			
Meth. Maint. & other	—	0 (0/217) (WB & IF)	[28] 1985
Denver			
Outpt. (Sexually transmitted disease clinic)	4 (—)	—§	[2] 1985
Detroit			
Hosp.	18 (17/96)	13 (12/96)	[29] 1985–86

The groups of IVDU studied in various locations are described more fully in the text (see Seroepidemiology, above).
*Detox.: Detoxification Program (in-hospital)
**Meth. Maint.: Methadone Maintenance Program (outpatients)
***Hosp.: Hospitalized (for reasons other than detoxification, usually infections)
****Outpt.: Outpatients
*****Meth. Maint. Admit.: Methadone Maintenance Program Admissions (outpatients)
§Confirmation of enzyme-linked immunoassay (EIA) seropositivity by a Western blot (WB), radioimmunoprecipitation with p25 (RIPA—p25), immunofluorescence (IFA), or other methods was not mentioned in the report

GEOGRAPHY OF THE EPIDEMIC

The epidemic of HIV infection among IVDU is more advanced in New York City than elsewhere in the U.S. The first series of reports describing AIDS in 1981–82 included one from New York City with a few cases in heterosexual male IVDU as well as homosexual/bisexual males [65]. Reports describing AIDS cases in female IVDU [66], among prisoners who had abused drugs [67–69], and in heterosexual IVDU presenting to a number of general hospitals [70–72] confirmed that intravenous drug use was a separate risk factor from homosexuality and bolstered the hypothesis that a blood-borne transmissible agent was etiologic. All these early reports were from metropolitan New York City, and to this date about 80 percent of the reported U.S. AIDS cases with intravenous drug use as the primary risk factor are in the New York City area. There has been an apparent link between New York City IVDU and homosexual/bisexual men. In one study, most of the IVDU with AIDS or AIDS-related complex (ARC) reported needle sharing with homosexual/bisexual men in "shooting galleries," sites where rented needles are re-used by multiple different IVDU [73]. While the exact origins of HIV remain obscure and it may have infected IVDU in the U.S. as early as 1971 [74], the New York City area has the highest reported seroprevalence among IVDU in the U.S., ranging from about 30 percent to over 60 percent WB-confirmed HIV seropositivity in recent studies (refer to Table 1).

The geographic spread of HIV in the IVDU population has apparently been more restricted than among homosexual/bisexual men, perhaps because of the limited mobility imposed by withdrawal symptoms and drug-seeking behavior. In 1984, a study of IVDU in New Jersey drug treatment programs (including methadone maintenance, outpatient drug-free, and residential treatment programs) found decreasing seropositivity rates with increasing distance from Manhattan ([21–23], Table 1). Fifty-nine percent (136/231) of those within five miles of Manhattan, 45 percent (75/166) of those five to nine miles from Manhattan, 24 percent (69/287) of those 10–35 miles from Manhattan and 1.6 percent (1/61) of those 80 miles from Manhattan were WB-confirmed HIV seropositives [21–23]. Preliminary data from surveillance of drug treatment program admissions in four different Connecticut metropolitan areas in 1986–7 also show that HIV seroprevalence decreases (from 41 percent to 14 percent) with increasing distance (from 38 to 113 miles) from New York City [25]. The epidemic is not strictly limited to one area, however, as evidenced by the seroprevalence among groups of IVDU in Boston, San Francisco, and numerous cities in Europe, particularly in Spain, Italy, Switzerland, France, and the United Kingdom (Tables 1–3). The epidemic may be spreading from urban centers with high prevalence to surrounding areas. In the absence of intervention, the pace of such an expansion of the epidemic may well increase as both the number of prevalent cases and number of high prevalence urban centers increase.

PACE OF THE EPIDEMIC

HIV seroprevalence in IVDU in several U.S. cities appears to be quite low at present (Table 1). If the experience in the locations where seroprevalence has been assessed serially over time is any indication, however, the potential explosiveness of this epidemic should not be underestimated. In New York City, New Haven, Edinburgh, Dublin [36], Valencia, Milan, Padua, and Bari (refer to Tables 1–3) seroprevalence has been observed to increase rapidly. In New Haven, the seroprevalence in a large, community-based, non-hospitalized sample has more than doubled between 1982–3

and 1986–7 to 25 percent [25], approaching the level of infection in the New York City area. The HIV seroprevalence among IVDU in drug treatment has increased in New York City from 11 percent in 1977 to 27 percent in 1979 and to 58 percent in 1984 [75]. Even more rapid spread has been noted in some European cities. In Edinburgh, confirmed HIV seroprevalence in two different study groups rose from 0 to more than 40 percent in two years [34,35]; in Spain [37,38] and Italy [49,50,53,54], increases from 0 to as high as 75 percent HIV EIA seroprevalence were noted over several years.

There are differences in frequency of needle sharing in different locations; 35 percent (122/353) reported sharing daily in New Jersey, 10 percent (21/218) reported sharing daily in New Orleans, and 5 percent (6/128) reported sharing daily in Washington, D.C. [23]. It is likely that HIV spreads more rapidly through the IVDU in a community at any given prevalence level if needle sharing is more frequent in that community than another. In London, for example, only 31 percent (14/45) of the IVDU interviewed reported needle sharing within the prior three months [33], but in Edinburgh 63 percent (49/78) reported sharing weekly, and 42 percent (33/78) reported sharing on a daily basis [76]. This difference may account for the lower reported seroprevalence in London compared to Edinburgh [76] and may help to explain the dramatic difference between the two cities in the increase in HIV seroprevalence from 1983–1985 (refer to Table 2), which suggests that large-scale reduction in needle sharing among IVDU might slow the spread of the epidemic.

RISK FACTORS FOR HIV SEROPOSITIVITY

Needle Sharing

Numerous studies suggest that the risk of HIV seropositivity in IVDU is correlated with the frequency of sharing needles [15,18,21,34,73,76] or sharing needles in a shooting gallery [18]. This risk factor may also be indirectly reflected in total duration of drug use, which has also been associated with seropositivity [18]. One study explicitly confirms the hypothesis inherent in all these data that there is an increasing risk of HIV seropositivity with increasing numbers of persons with whom needles are shared [27].

Race/Ethnicity

In the U.S., the cumulative incidences of AIDS among blacks and Hispanics are each over three times the rates for whites [77]. The Northeast exceeds the national average, however; the incidences of AIDS among Connecticut blacks and Hispanics are each nine times the rate for Connecticut whites [78]. Eighty-one percent of the reported U.S. AIDS cases in IVDU, 72 percent of women with AIDS, and 90 percent of children with perinatally acquired pediatric AIDS are black or Hispanic [77]. While the proportion of AIDS patients who are black or Hispanic is greatest among those with IV drug use as their primary risk factor, the proportion of blacks and Hispanics with AIDS is relatively high (compared to the overall population's racial/ethnic distribution) in all transmission categories, except hemophiliacs [77].

Indeed, HIV seroprevalence studies in the U.S. have revealed a racial/ethnic group association with HIV seropositivity that parallels the patterns of reported AIDS cases. Among the military recruit applicants surveyed for HIV antibody, there was a fourfold higher seroprevalence among the blacks compared to the whites [6]. One group of

TABLE 2
HIV Seroprevalence Among IVDU[a]

Location/Group	% EIA + (No.)	% Confirmed + (No.)	[Ref] Date
London, U.K.			
—	1.5 (4/269)	1.5 (4/269) (IF)	[30] 1983–84
—	2.5 (5/203)	2.5 (5/203) (IF)	[31] 1984
—	—	6.4 (15/236) (IF)	[32] 1985
—	0.7 (1/146)	—§	[33] —
Edinburgh, U.K.			
—	—	51 (83/164) (WB & IF)	[34] 1981–85
Hosp.	—	0 (0/182) 1982 (WB & IF) 14 (17/124) 1983 42 (86/205) 1984 37 (66/178) 1985	[35] 1982–85
Dublin, Ireland			
—	—	0 1982 (WB) 30 (178/603) 1985	[36] 1982–85
Valencia, Spain			
—	37 (112/303) 11 1,983 40 1984 48 1985	—	[37] 1983–85
Bilbao, Spain			
—	50 (239/479)	27 (131/479) (WB)	[38] 1984–85
Barcelona, Spain			
Hosp.	—	71 (82/115) (IF)	[39] 1985
Madrid, Spain			
Hosp.	—	64 (—) (WB & IF)	[40] 1985
Barcelona, Spain			
Hosp.	56 (53/94)	—§	[41] 1984–85
Amsterdam, The Netherlands			
Meth. Maint. Admit.	3 (5/145)	—§	[42] 1983–84
Prostitutes	23 (12/52)	—	[42] 1983–84
Stockholm, Sweden			
—	40 (—)	—§	[43] 1985
Zurich, Switzerland			
—	—	36 (37/103) (WB)	[44] 1984
Geneva, Switzerland			
—	52 (68/131)	—§	[45] 1981–85
Bern, Switzerland			
—	—	42 (16/38) 1984 (IF) 32 (12/37) 1985 (IF)	[32] 1981–85
Munich, W. Germany			
—	—	4 (5/128) 1983 (IF) 6 (4/62) 1984	[46] 1983–84
West Berlin, W. Germany			
Prisoners	>50 (—)	—§	[47] 1980–85

[a]Refer to footnotes of Table 1.

potential blood donors had a sevenfold greater seroprevalence among blacks than whites [83]. The HIV seropositives in this sample of voluntary blood donors were largely (82 percent) in the homosexual transmission mode category [79]. The data from seroprevalence studies of U.S. IVDU uniformly show at least a two- to fourfold higher seroprevalence among blacks and Hispanics [14,18,25,27] than among whites.

In New York City [14,18,80], New Jersey [21], San Francisco [27], and Connecticut [25], HIV infection is more prevalent among black and Hispanic IVDU than among white IVDU in large, non-hospitalized study groups drawn from outpatient drug treatment programs. This racial/ethnic group association with HIV seropositivity has not been reported among European IVDU. The increased risk of HIV seropositivity for black and Hispanic IVDU appears greater in the Connecticut sample than in the other groups of IVDU that have been studied. The Connecticut IVDU studied on entry to drug treatment programs were mostly white (76 percent) [25]. In New Haven in 1986, 82 percent of the blacks and 40 percent of the Hispanics entering the drug treatment programs were seropositive, while only 10 percent of the whites entering the same programs were seropositive [25].

There is no clear explanation for these observations yet. The differences in prevalence by racial/ethnic group do not simply reflect the racial/ethnic group distribution of the IVDU population at risk for HIV transmission. The increased risk of HIV acquisition among black and Hispanic IVDU seems likely to be due to more frequent needle sharing with different individuals among blacks and Hispanics, possibly because of educational and/or socioeconomic factors. There was only a minimal suggestion of differences in needle-sharing practices in only one of the relevant studies, however, in which univariate analysis revealed that more whites (18 percent) than blacks (8 percent) reported using sterile needles at least half the time [18]. Therefore, it is also possible that racial/ethnic group (or socioeconomic) differences may be correlated with a higher prevalence of a behavioral risk factor (i.e., specific injection practice) or a pathogenetic cofactor that increases the efficiency of HIV transmission. Viruses that may act as cofactors for HIV by increasing the likelihood of a productive infection upon HIV inoculation may be more prevalent among U.S. blacks and Hispanics. Herpesviruses, such as human cytomegalovirus (CMV) or Epstein-Barr virus (EBV), or other retroviruses, such as human T-lymphotropic virus, type 1 (HTLV-I), might be hypothesized to play such a role. Case clustering (i.e., strictly intra-racial needle sharing) seems unlikely to account for the association with racial/ethnic group in New Haven based on reports of former addicts. A genetic predisposition to HIV infection among blacks must be considered, but may not be a plausible explanation, given the high HIV seroprevalence rate among Hispanics as well. Even before the necessary studies are done to determine the aspect of the human biology of HIV that is responsible for this phenomenon, it is vital to target educational efforts to blacks and Hispanics, as well as IVDU in general. The risk of HIV transmission will be greater when injection equipment is re-used after an initial use by a member of a higher prevalence IVDU sub-group; i.e., blacks and Hispanics.

MODES OF HIV TRANSMISSION

The likelihood of HIV transmission with each encounter with an infected person may vary in different kinds of sexual, and non-sexual bloodstream, encounters. In homosexual/bisexual men, a number of studies have pointed to specific sexual practices (particularly receptive anal intercourse [81,82]) that increase the risk of

acquiring HIV. Guidelines for the education and counseling of homosexual/bisexual men have been based on such studies. Similar information about injection practices and heterosexual intercourse would be useful in optimizing educational campaigns for AIDS risk reduction among IVDU, might lead to new strategies in the difficult battle against drug abuse, and will help to predict the future extent of the spread of HIV among needle-sharing IVDU and from IVDU to their heterosexual partners.

While little data exist to quantitate relative risks, sexual contact seems a less common mode of transmission among IVDU than the re-use of HIV-contaminated injection equipment. One report of stable heterosexual couples in Italy found concordant HIV seropositivity in 58 percent (7/12) of the couples where both were needle-sharing IVDU, but in only 8 percent (1/12) of the couples where only one partner was an IVDU [83], suggesting that sexual intercourse was a less efficient means of HIV transmission than needle sharing. Nevertheless, concern about spread by heterosexual contact from IVDU to those who do not consider themselves at risk for HIV infection is warranted. Forty-eight percent (20/42) of the heterosexual partners of New York City IVDU with AIDS or ARC were HIV-seropositive [84]. While male-to-female heterosexual transmission is firmly established and primarily related to acquisition from IVDU [85] in the U.S., the controversy about the extent (and relative efficiency) of female-to-male sexual transmission of HIV in the U.S. continues [86–89]. The need for longitudinal studies to compare the incidences, duration of infectiousness, and course of HIV-related disease among heterosexual couples who have discordant drug abuse habits (that is, sexual but not needle-sharing contact) remains acute to assess fully the potential for expansion of the epidemic from IVDU to the non-drug abusing U.S. population.

The role of specific injection/needle-sharing practices in the acquisition of HIV by IVDU is also of public health interest. There is little knowledge about how IVDU inject drugs, but former addicts report extensive use of "hitters" (person who find a vessel for injection for a fee without regard for sterile technique), "booting" (rinsing the last remnants of drug from syringes by drawing blood in and out of the shared syringe several times), and common "cookers" (from which solubilized drug is drawn up for "booting" into many different individuals' syringes, allowing admixture of blood from different individuals in the "cooker"). Such descriptions suggest that some injection practices may be highly efficient at transmitting HIV, but the descriptions are not sufficient to reveal the real environment in which HIV is spreading in the isolated world of IVDU. It remains possible that specific injection practices help determine which needle-sharing IVDU acquire HIV.

Needle sharing is deeply embedded in the drug abuse subculture and seems to serve both social and economic purposes. Both "works" (syringe, needle, and other equipment) and drugs are often shared between "running buddies" who cooperate to obtain drugs. Refusal to share "works" and/or drugs might be interpreted in that context as an attack on the only bond of friendship in a world dominated by mistrust, fear, and violence. It is common for IVDU to rent works at the time of drug purchase, especially in those states with criminal penalties for drug paraphernalia possession. The works may also be shared because withdrawal symptoms, apathy, or inconvenience limit the attempts to get an available sterile needle. There is also an economic variable, as needles may not be available or affordable for purchase. Similar reasons for needle sharing have been reported from many locations, including areas with low HIV seroprevalence such as Dallas [90] and Sydney [61].

Several studies have shown that almost all the IVDU interviewed in 1984–86 in New York City, New Jersey, and Connecticut do know that needle sharing and sexual intercourse are the modes of acquisition of AIDS [91–94]. There is also considerable reported behavioral change: about 60 percent of the respondents of two New York City studies [91,92] attempted to reduce hazardous injection practices by stopping or decreasing needle sharing, stopping IV drug use, or attempting to sterilize needles. In another study in New Jersey, almost half said they were entering drug treatment because they were afraid of AIDS [93]. Ethnographic evidence from New York City suggests that IVDU may be attempting to protect themselves from HIV infection: the ilicit market for sterile needles has increased, some drug dealers have distributed "free" works as a marketing technique, and some fraudulent street sale of used, re-sealed needles as new has occurred [95,96]. Among those being admitted to drug treatment programs in New Haven in 1986 [94], most (65 percent) had shared needles; most said they shared with friends and acquaintances, and very few reported sharing with strangers (as has been noted in Dallas [90]). Almost all of the New Haven sample (97 percent) attempted to clean shared needles, albeit probably ineffectively by rinsing with tap water [94]. In San Francisco, almost all the IVDU interviewed cleaned needles prior to injection, but less than 20 percent of these used methods effective for HIV decontamination, such as boiling or alcohol [27]. In that study, a protective effect of needle cleaning on HIV seropositivity was not seen [27]. The public health policy implications of this recognition of the modes of transmission of HIV and possible attempts to interrupt such transmission by IVDU will be discussed below.

NATURAL HISTORY OF HIV INFECTION IN IVDU

A better understanding of why AIDS (or other clinical manifestations) develops within a few years in some HIV-infected persons and not others is necessary to estimate the full impact of the HIV epidemic. The extent of the future spread of the HIV epidemic depends largely on a complex interplay of still unknown parameters—the degree and duration of infectiousness and life span of HIV-infected persons [97]. The clinical outcome after infection with HIV may be anywhere along a continuum of increasing immunodeficiency that has been arbitrarily divided into asymptomatic infection, generalized lymphadenopathy, AIDS-related complex (ARC), and AIDS [98–100]. (Neurologic disease also occurs but often is unassociated with manifestations of immunodeficiency and may be due to different pathogenic processes.) A copy of HIV genetic material is presumed to remain integrated in the genome of infected human cells for life. The "incubation period" from time of infection to onset of disease and the percentage of infected persons that ultimately develop illness remain undefined, largely because of the limited observation period (since 1981). Both parameters have increased with the length of observation, however. It is hypothesized that the clinical manifestations of HIV infection are due to progressive depletion of the major cell type that supports cytopathic HIV replication—the T-helper lymphocyte.

While many large cohorts of homosexual/bisexual males have been studied to determine the natural history of HIV infection, only a few groups of IVDU have been studied. Small samples, short periods of follow-up, and lack of knowledge of duration of infection for prevalent HIV seropositives limit these data from groups of IVDU. The longest follow-up to date—from 1982 to 1985—includes only 29 percent of a group of 24 New York City IVDU who were HIV-seropositive on entry [101]. Two IVDU from this group (at least 8.3 percent of the cohort) had developed AIDS by 1985 [101]. A

larger sample from New York City (166 HIV-seropositives) was followed for a shorter time (nine months in 1984–85) with a 4 percent annualized rate (5/166) of developing AIDS [16]. While 54 percent of this group initially had normal absolute T-helper lymphocyte (T4-positive cell) counts, 26 percent of the group had T4-positive cell counts that decreased to below normal over nine months, suggesting progressive HIV-related disease [16]. Another group of 36 HIV-seropositive New York City IVDU followed for one year (1984–85) included 8.3 percent (3/36) who developed AIDS over that year and 25 percent (9/36) who had generalized lymphadenopathy on initial presentation [19]. In Geneva [45], 42 HIV-seropositive IVDU were followed for an average of 28 months after seroconversion with a risk of developing AIDS of only 0.14 percent; however, 69 percent of this group developed generalized lymphadenopathy. Similar data on the high frequency of generalized lymphadenopathy in HIV-infected IVDU has been presented from Edinburgh [35] and is consistent with the clinical impression and preliminary data gathered in New Haven as well. Data from homosexual/bisexual cohorts suggest, however, that generalized lymphadenopathy may not be a stable, long-term outcome after HIV infection; the risk of developing AIDS continues for up to five years after onset of lymphadenopathy without decreasing [102].

Markers that are predictive of HIV-related disease progression, whether or not they determine the outcome, have been sought in epidemiologic studies. Unexplained oral candidiasis was often found to be the first manifestation of AIDS, preceding the development of serious opportunisitic infections more than 50 percent of the time in previously healthy New York City IVDU [103]. The most strongly predictive markers for progression defined in homosexual/bisexual cohorts are: decreases in the number of T-helper lymphocytes [104], decreases in antigen-stimulated lymphocyte proliferation and gamma-interferon generation [105], and a progressive loss of antibody to an HIV virion core protein (anti-group specific antigen [*gag*, p24] antibody) [44,106,107]. In one large prospective study, a number of factors were found to predict outcome independently among the prevalent homosexual/bisexual HIV-seropositives: increased T-suppressor/cytotoxic cell number, decreased T-helper cell number, reduced amount of serum HIV antibody (defined as reactivity in optical density units on a commercial EIA for HIV), an increased amount of serum CMV antibody (possibly reflecting recent, active CMV replication), and a history of sexual contact with someone who developed AIDS [108]. The last factor listed is of interest since it suggests either that this exposure variable reflects longer-standing HIV infection, that some strain variation exists in the pathogenicity of HIV, or that another cofactor (such as another virus) is involved in the pathogenesis of AIDS.

In vitro studies have also suggested a number of variables that might determine the outcome after HIV infection. Antigen (or mitogen) stimulation of T-helper cells *in vitro* enhances the efficiency and productivity of what would otherwise be a latent HIV infection [109,110]. The transcription of latent HIV long terminal repeat-linked genes (that are integrated into the host cell genome) is dramatically increased *in vitro* after herpes simplex [111,112], varicella zoster, papillomavirus, or papovavirus [112] infections. It seems possible that chronically repeated *in vivo* activation of the immune system (by other infections or by the allogeneic stimulation of needle sharing) may improve the chances of establishing an HIV infection after exposure and also shorten the length of the period from HIV acquisition to disease onset. Another possible factor in the pathogenesis of HIV-related disease in IVDU is the potentially immunosuppres-

sive effect of opiates. Opiates impair *in vitro* T-cell mitogen responsiveness [113,114], an effect which is reversed by naloxone [113].

Given such epidemiologic and biologic data, the finding that continued IV drug injection was associated with greater decreases in T-helper lymphocyte counts in a cohort of IVDU followed over nine months [16] strongly suggests that disease progression was due to one or more of a number of possible factors: immunosuppression from the drugs injected, antigenic stimulation from other injected microbes or other individuals' cells, reinfection with HIV of the same or different strain, or infection with another virus that may activate latent HIV (or increase the productivity of an HIV infection). Further studies of HIV-infected IVDU may help to separate some of these possible factors and expand knowledge of the pathogenesis of AIDS.

When HIV infection has progressed to AIDS, IVDU may have a worse prognosis than persons in other HIV transmission categories. IVDU with AIDS rarely present with Kaposi's sarcoma and usually develop multiple opportunistic infections; survival figures reflect the fact that IVDU have more rapidly fatal manifestations of immunodeficiency. Whether these differences are due to different pathogenetic processes resulting in more severe immunosuppression after parenteral rather than rectal mucosal inoculation of HIV remains conjectural. Much of the apparent excess morbidity among HIV-infected IVDU (compared to persons in other HIV transmission categories) may be related to socioeconomic rather than biologic variables; health knowledge and access to health services are less than optimal among IVDU. In order to explain the much lower prevalence of Kaposi's sarcoma cases among AIDS patients outside of the homosexual/bisexual HIV transmission mode category, it has been hypothesized that homosexual/bisexual men are more likely than persons in other HIV transmission mode categories to be exposed to another cofactor (possibly an unidentified virus transmitted by semen) that leads to Kaposi's sarcoma [104].

The increases in premature mortality related to AIDS are already considerable in New York City and most marked among blacks and Hispanics [115]. In addition to increases in deaths due to AIDS among IVDU, a large increase in narcotic-related deaths due to pneumonia has been seen in New York City, while other causes of mortality in IVDU (i.e., overdose, cirrhosis, and so on) have not changed [115]. Infection with *Mycobacterium tuberculosis* is also a growing problem among HIV-infected persons [72,116–119], particularly among urban IVDU. In 1985, the national average annual decline in tuberculosis morbidity (expected to be about 5 percent) did not occur [116], and in some areas, such as Florida and Connecticut, the incidence increased [117,118]. Severe and unusual presentations of *Mycobacterium tuberculosis* infection may precede the diagnosis of AIDS among those at risk for HIV infection, although the response to standard therapy appears good [119]. IVDU are also prone to acquire other infections, such as endocarditis and soft-tissue infections. Two studies have noted an association between HIV seropositivity among IVDU and such non-opportunistic infections [29,120]. It seems likely that this association represents selection bias toward those whose more intensive drug injection habits lead to both greater HIV exposure and other injection-related infections, but HIV-induced immunosuppression may predispose to such non-opportunistic infections. Bacteria that are prominent pathogens in B-cell deficiency states, such as *Hemophilus influenzae* and *Streptococcus pneumoniae,* have been described as etiologic agents of pneumonia among HIV-infected persons [121], and such pathogens might be expected to be successful opportunists at other body sites in HIV-infected IVDU as well. Thrombocy-

topenia often precedes other manifestations of HIV infection and may have a different pathophysiology in IVDU than in HIV-infected homosexual/bisexual men [122]. The finding of antibody to HTLV-I (and HTLV-II) among stored sera from New York City IVDU [14] raises the specter of retrovirus-related malignancy (and possibly as yet undefined interactions with HIV) among IVDU. The full impact on the public health of the epidemic of HIV infection among IVDU cannot yet be assessed, but it clearly will not be limited to what is currently the Centers for Disease Control (CDC) case definition of AIDS.

PUBLIC HEALTH POLICY IMPLICATIONS

The public health is threatened by this developing epidemic to an extent that is unsurpassed in recent history. The U.S. Public Health Service (USPHS) projects that by 1991 approximately 270,000 individuals will have developed AIDS, with projected medical care costs of $16 billion [123]. If present trends continue, many of these cases will occur among the socially disadvantaged, and the burden in social disorganization and economic cost to the public treasury will be staggering. More research is necessary to estimate accurately the full extent of the future problem and to develop optimal strategies for intervention at the level of both transmission and disease progression. Planning to allow IVDU greater access to medical, nursing, and social service resources must begin. The major immediate need, however, is for action to stop this epidemic by eliminating drug injection or, at the least, stopping IVDU from re-using potentially HIV-contaminated injection equipment.

The most effective public health response at this time would be primary prevention of drug abuse. Adolescents at the junior and senior high school level are the most likely to begin experimentation and regular use of addictive drugs; campaigns directed at this age group might be effectively increased [124]. It may well be beneficial to link the "war on drugs" with the "war on AIDS." Discussions of the realities of drug addiction and AIDS with young people might discourage experimentation. Indeed, one survey of Connecticut senior high school students found that the students knew very little about AIDS and drug abuse [2]. The students were particularly unaware of the transmission of AIDS to the children and heterosexual partners of drug abusers [2]. In one Italian community, a striking fall in admissions for acute viral hepatitis and an increase in applicants for methadone maintenance drug treatment has been recorded in 1985–86 [125]. Since acute viral hepatitis is usually acquired during the first 18–24 months of heroin abuse, this suggests the possibility of fewer new IVDU in that community in response to a fear of AIDS [125].

The approach to those who are already addicted is more problematic, but the goal should be to stop IVDU from injecting drugs. Current drug addiction treatment programs are limited in capacity and not always successful at eliminating IV drug injection. It is common for drug addiction to take a chronically relapsing and remitting course with successive treatments followed by longer remissions [126]. Indeed, injection drug use may not cease while an addict is in treatment. Thus, simply expanding U.S. drug treatment programs (largely chronic outpatient methadone maintenance with extensive counseling/rehabilitation services) to accommodate all applicants immediately (instead of the current one- to six-month waiting periods for program entry in many cities) may not decrease transmission of HIV among IVDU. Decreasing drug injection, however, or stopping for a time might be expected to interrupt the natural history of HIV infection and potentially prolong the time to (or

prevent the development of) illness by any one of a number of potential mechanisms discussed above. These hypotheses are currently under study in New Haven by comparing the incidence and natural history of HIV infection in IVDU who have been stable on methadone maintenance with those who have failed treatment.

If drug injection by IVDU cannot be stopped, a major effort to eliminate needle sharing may be the most effective way to halt this epidemic. In Amsterdam, a needle exchange program that allows IVDU to obtain sterile syringes and needles in return for used ones has been in operation for about two years. The goal is to stop needle sharing by making sterile needles readily available, but an evaluation of the program's effectiveness toward that end has not yet been published. Britain is also setting up a small pilot needle exchange program, and both France and Switzerland recently moved to allow the over-the-counter sale of syringes and needles in pharmacies [127]. It is of interest that syringes have been available in Italian pharmacies without prescription for some years, and HIV seroprevalence has risen swiftly among Italian IVDU (refer to Table 3).

In the U.S., there have been suggestions for programs akin to the Dutch attempts to provide sterile needles and syringes to IVDU. The possibility of fostering drug abuse by making it easier to acquire injection paraphernalia and the lack of proof that a needle exchange program would alter the pervasive needle-sharing behaviors of IVDU has prevented these proposals from gaining favor. The social, legal, educational, and financial impediments to supplying sterile needles to IVDU in the U.S. are considerable, and evidence of the effectiveness of existing needle exchange programs seems necessary before such a plan can be seriously considered.

State legislative bodies, however, might consider a different approach to decreasing needle sharing without awaiting further data. The criminal penalties for possession of drug injection paraphernalia might be adjusted to reflect more accurately society's current interest. It might be reasonable to attempt to enforce more stringent penalties for possession of used (or re-sealed) needles or multiple needles than the possession of one sterile needle. The possibility of decriminalization of injection equipment possession might also be discussed as an alternative to providing sterile needles that would not make it easier for young persons to begin to abuse IV drugs. One major motivation for needle sharing might be removed by eliminating the criminal penalty for addicts to carry their personal "works."

The HIV epidemic among IVDU in the U.S. might be interrupted immediately, however, by encouraging the existing trend among IVDU to clean shared needles, as described above. While most IVDU do not use methods known to inactivate HIV, effective methods could be taught. Boiling or using alcohol are impractical methods that IVDU have not accepted; the former is impossible in the addicts' environment, and some former addicts report that alcohol destroys the lubricant in disposable syringe plungers, making the syringe unusable [personal communication]. Careful virologic studies of alternative needle-cleaning methods have not yet been reported. In San Francisco and other locations, however, IVDU have been more accepting of using household bleach (sodium hypochlorite) to clean needles. An innovative marketing approach has clearly helped to get the message across (Fig. 1). Pocket-sized, refillable bottles with cartoon instructions on use can be introduced into the needle-sharing setting much less awkwardly than an IVDU can refuse to share works with a "running buddy." As the developers of the concept say, the "bleach bottle" is the "moral equivalent of the condom." Like the condom, this approach to risk reduction requires

TABLE 3
HIV Seroprevalence Among IVDU[a]

Location/Group	% EIA + (No.)	% Confirmed + (No.)	[Ref] Date
Innsbruck, Austria			
Prisoners	—	44 (15/34) (WB & IP)	[48] 1985
Milan, Italy			
Meth. Maint. & Hosp.	—	29 (61/209) 1985 0 1979–80 (IF)	[49] 1979–85
Residential treatment	—	53 (33/62 1984–5 7 1981 (IF)	[49] 1979–85
Hosp.	30 (212/716) 7 1979 22 1982 60 1985	—§	[50] 1978–85
Rome, Italy			
—	—	20 (26/128) (IF)	[51] 1985
Meth. Maint.	—	28 (58/207) (IF)	[52] 1985
Padua, Italy			
Hepatitis study	21 (79/382)	16 (60/382) (WB) 0 1978–79 1.4 1981 15 1983 43 1985	[53] 1978–85
Bari, Italy			
Hepatitis study	0 (0/129) 1978–79 6 (4/68) 1980 10 (6/58) 1981 15 (7/47) 1982 31 (15/49) 1983 53 (18/34) 1984 76 (45/59) 1985	—§	[54] 1978–85
Toulouse, France			
—	51 (205/402)	—§	[55] 1985
Tours, France			
Hosp.	—	0 (0/52) 1982–83 (WB) 15 (10/40) [*sic*] 1984 17 (21/125) 1985	[56] 1982–85
Paris, France			
Prisoners	—	64 (71/113) (WB)	[57] 1985
Athens, Greece			
Prisoners	—	2 (6/288) (WB)	[58]—
Belgrade, Yugoslavia			
—	45 (111/244)	45 (10/22 EIA+'s) (WB)	[59] 1985
Zagreb, Yugoslavia			
—	6 (9/142)	6 (9/142) (WB)	[60]—
Sydney, Australia			
—	2 (2/100)	—§	[61]—
Thailand			
—	0 (0/99)	—	[62] 1985
Hong Kong			
—	0 (0/508)	—	[63] 1985
Tamilnadu State, India			
—	0 (0/14)	—	[64] 1987
Prostitutes (?IVDU)	5 (50/1,025)	3 (30/1,025) (WB)	

[a]Refer to footnotes of Table 1.

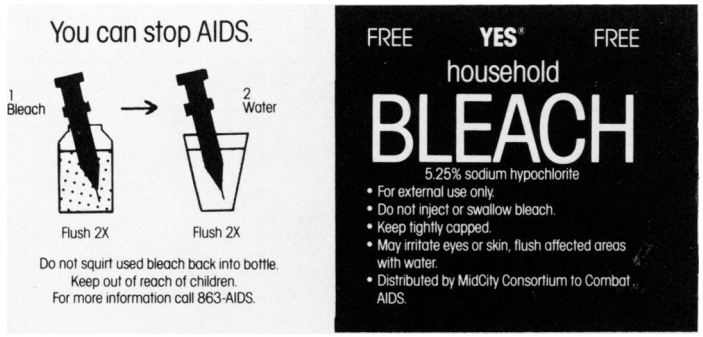

FIG. 1. The "bleach bottle" label. One-ounce, refillable bottles of household bleach (sodium hypochlorite) have been widely distributed among San Francisco IVDU by indigenous addict-educators for de-contaminating shared injection equipment of HIV prior to drug injection.

absolute consistency in order to be effective. There is also the possibility that sharing of other injection paraphernalia (i.e., the "cooker") might make futile the effects of needle cleaning.

The use of indigenous addict-educators (largely former and present addicts) may be the best available approach to disseminate needle-cleaning and other health educational material to the isolated, stigmatized, untrusting IVDU subculture. The undetermined proportion of IVDU who are not in drug treatment programs will probably not be reached by any other means. The "bleach bottle" was introduced by street-wise field workers in San Francisco, and a similar approach to IVDU education has been ongoing in New York City [92] and New Jersey [93].

It is now crucial to offer individualized, in-depth counseling about HIV infection to IVDU in all drug addiction treatment programs in the U.S. Voluntary, confidential HIV screening may be a useful adjunct to such an effort. Whether an individual IVDU's knowledge of an HIV antibody test result will be conducive to a socially beneficial behavioral change remains at issue, however. For example, a seropositive IVDU may decide that there is nothing to lose by continuing drug injection and needle sharing. An IVDU found to be seronegative may take false assurance that his particular practices (i.e., needle sharing only with friends or cleaning needles with tap water, for example) are effectively protecting him or her from HIV infection and continue such clearly dangerous practices. A number of studies (see above) do suggest that IVDU are capable of, and interested in, decreasing their risk of HIV infection. The most effective way to motivate IVDU to reduce their risk of HIV infection and its progression to AIDS remains to be determined. Screening all pregnant IVDU (and women whose sexual partners are IVDU) for HIV seropositivity also seems useful for the psychological well-being of the mother and the health of the expected infant. It also seems reasonable to screen clients from known HIV transmission categories in long-term psychiatric institutions for HIV seropositivity and potentially cohort together the seropositives if there is any risk of sexual or needle-sharing contact among such clients.

A much larger effort to educate the general public as well as IVDU about HIV-related health issues is also needed. Until now, AIDS educational efforts have been aimed at the largely white, well-educated, homosexual/bisexual community. The racial/ethnic groups at greatest risk for HIV infection and AIDS must be reached with

the message that needle sharing and heterosexual (as well as homosexual) activity with an IVDU carry a risk of acquiring HIV. In order to avoid fueling ugly bigotry, much of which has already been directed toward homosexual/bisexual men, it is necessary to inform the public fully and explicitly in regard to the scientific certainties about the lack of HIV transmission by means other than unprotected sexual and bloodstream contact.

Limitation of the spread of HIV within IVDU and to their sexual contacts and children ought to be a high social priority. Historically, drug abuse has, however, been a persistent and perplexing problem for our society. As the International Working Group on AIDS in IVDU emphasized in June 1986, "the extraordinary nature of this epidemic demands comprehensive and creative responses" [128]. All pragmatic measures, no matter how controversial, should be considered in mobilizing against this threat. Protection of the public health from this "social" disease can be effected through sociocultural, as well as immuno-pharmacologic, advances. Indeed, as Mathilde Krim has stated in a more general context, how societies "will deal with the threat of AIDS will measure to what extent they have the right to call themselves civilized" [129].

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